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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,701	05/16/2001	Benjamin P. Warner	S-94,661	4132
35068 7590 09/30/2008 LOS ALAMOS NATIONAL SECURITY, LLC LOS ALAMOS NATIONAL LABORATORY P.O. BOX 1663, LC/IP, MS A187 LOS ALAMOS, NM 87545				
EXAMINER				
FOSTER, CHRISTINE E				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/859,701

Applicant(s)

WARNER ET AL.

Examiner

Christine Foster

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- 7) ☐ Paper No(s)/Mail Date: _____

DETAILED ACTION

Amendment Entry

1. Applicant's amendment, filed 6/30/08, is acknowledged and has been entered. Claims 1 and 11 were amended. Claims 1-20 are pending and subject to examination below.

Priority

2. The present application was filed on 5/16/2001. No priority claims have been made.

Objections/ Rejections Withdrawn

3. The rejections of claims 1-10 under § 112, 1st paragraph have been withdrawn in response to Applicant's amendments to claim 1.
4. The rejections under § 112, 2nd paragraph as set forth in the previous Office action have been withdrawn in response to Applicant's amendments to claims 1 and 11.
5. The rejections of claims 1-8, 10-18, and 20 under 35 U.S.C. 102(b) as being anticipated by Wang (US 4,663,277) in light of Plester et al. (US 4,830,192) have been withdrawn in response to Applicant's amendments to claims 1 and 11 to recite that the plurality of receptors is "unbound" and that "bound" receptor is separated and arrayed onto the substrate.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

8. Claims 1 and 11, as instantly amended, recite exposing a plurality of “**unbound**” receptors to at least one binder in step (a). Applicant's reply does not indicate where support may be found for the limitation that the receptors are “unbound”, and the Examiner was unable to find support in the specification or claims as originally filed for the following reasons.

The specification does not employ the terminology “unbound”. When the claim terminology “unbound” is given its broadest reasonable interpretation, receptors that are “unbound” would encompass not only those receptors that have not yet been bound to the binder, but also receptors that are not bound to or in contact with any other type of biomolecule or material. However, in all of the examples disclosed in the instant specification, the receptors were provided *bound to beads* (see, e.g., page 8, line 15). Because all of the disclosed examples involved receptors that would reasonably be considered to be *bound* to beads in this manner, the specification fails to convey evidence of possession of methods in which a plurality of *unbound* receptors are exposed to binder.

9. Claims 1 and 11, as instantly amended, recite the step of “**separating said bound receptor**” in part (b) of the claims. It appears that the noted step has apparently been introduced into the claim in order to address the Examiner's rejection of the claim under 112, 2nd paragraph

as set forth in the previous Office action, in which the Examiner noted the absence in the claims of a step, e.g. a wash step, in which unbound binder is removed (see Applicant's Reply on page 7, part B). However, Applicant is reminded that all amendments or claims must find descriptive basis in the original disclosure, or they involve new matter. See MPEP 608. In the instant case, no support could be found for a step of separating the bound receptor as recited, and Applicant's reply does not indicate where support may be found.

The specification discloses examples of separation steps in which bead-supported receptors were exposed to potential binders and then washed prior to arraying on a substrate (see, e.g., page 6, lines 15-23). This washing step therefore separates *beads* from the sample; the receptors bound to the beads would still be retained regardless of whether they are bound to a binder or not. However, "separating said bound receptor" would read on separation steps in which only those receptors that are bound to binder are selectively separated from other components in the sample (e.g., not only to unbound binder but also to bead-supported receptors that are not bound to binder). No support could be found in the specification and claims as originally filed for such a scenario.

In addition, the specification, in disclosing only steps of *washing* bead-supported receptors, does not provide adequate support for the generically claimed step of "separating". No methods of separating bound receptors are disclosed (as noted above) and no methods of separating other than via *washing* are exemplified.

For all of these reasons, the specification fails to convey evidence of possession of the claimed subject matter.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 1 and 11 recite the limitation "said bound members" in part (d). There is insufficient antecedent basis for this limitation in the claims as there is no prior mention of a bound "member".

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-5, 9-15, and 19-20 rejected under 35 U.S.C. 102(e) as being anticipated by Sano et al. (US 6,391,590 B1).

Sano et al. teach methods of determining metal-binding activity of streptavidin-metallothionein chimeric protein, in which the receptors (i.e., chimeric proteins) are exposed to at least one potential binder, namely the metal ion Cd^{2+} which is provided as CdCl_2 during the

course of protein purification (Example 2, see especially column 15, lines 11-16 and 30-42; and also at column 2, lines 40-54). The reference further teaches spotting (i.e. arraying) the proteins onto a substrate (polypropylene membrane). See Example 3, in particular at column 15, lines 58-61). The arrayed proteins were then subjected to quantitative X-ray fluorescence in order to determine the amount of metals in the sample spot (Example 3). This reads on the instantly claimed step of detecting an X-ray fluorescence signal generated by the detectable element, since the signal of the deposited protein-bound heavy metal ion (cadmium) is measured thereby. See also column 2, lines 55-67. Regarding the limitation that the receptor is "unbound" and then arrayed in "bound" form, the chimeric protein of Sano et al. would be considered to be initially unbound before it is contacted with the metal ion during dialysis. When the sample is then spotted onto a membrane after the dialysis step, protein bound to Cd^{2+} would be arrayed. See column 15. By this process, unbound metal ion would be separated from bound and unbound receptor.

With respect to claims 2-5 and 12-15, the chimeric protein taught by Sano et al. reads on the instant claims as proteins are carbon-containing polymers of amino acids.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1-8, 10-18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (US 4,663,277).

Wang teach methods for detecting viruses and/or proteins, in which a plurality of viruses or proteins (i.e., receptors) in a specimen is exposed to an extended solid phase component (i.e., substrate) which is coated in at least one location with antiviral or antiprotein antibody (see especially the abstract; column 2, lines 16-67; column 3, lines 25-57; and claims 1, 20, and 39-40 in particular). This step in which viruses in the sample are bound to the solid phase via the antiviral or antiprotein antibodies reads on the claimed step of "arraying" the receptors on a substrate when given its broadest reasonable interpretation. For example, Wang teaches a solid phase that is a dipstick having two locations at which the antibody is coated (see Figure 3 and column 3, lines 65-68), such that the viruses would be bound to the dipstick in an array or pattern corresponding to the locations at which the antibody is coated. Different viruses can also be detected simultaneously by using different antiviral antibodies (column 7, lines 39-51), which would also be considered to represent an array absent a specific or limiting definition for this term.

Wang further teaches exposing the arrayed receptors to at least one potential binder, namely the same antibody coated onto a mobile solid phase of dispersed microspheres (see in particular column 2, lines 53-59; column 4, line 61 to column 5, line 2). In one embodiment, the microspheres in the binder may be doped with metal elements so as to enable detection by X-ray fluorescence using appropriate detection equipment (column 6, lines 12-20; column 7, lines 21-59; and claims 1 and 20, for example). The antibody-coated microspheres doped with metal elements therefore read on the instantly claimed "binder having an element detectable by X-ray fluorescence". Detection of the X-ray fluorescence of the metal element labels in the microspheres indicates that binding between the receptors and the solid phased antibody(ies) has occurred (i.e., detecting an X-ray fluorescence signal generated by the detectable element in the bound microspheres). See also claim 20.

Furthermore, the virus or protein receptors of Wang would be considered to be "unbound" when they are exposed to antibody-coated microspheres in the absence of a specific or limiting definition in the specification, in that they are not yet bound to the mobile particles. In particular, because the instantly disclosed embodiments involve the use of receptors which are bound to beads, the terminology "unbound" can be reasonably interpreted in this manner and is not seen to limit the claims to those receptors which are not bound to *any* other material or molecules, for example.

Wang further teaches of separating the solid phase substrate from the specimen and from unbound microspheres by washing (column 2, lines 60-63; and claims 4 and 20 in particular). Since the solid phase substrate contains bound receptor, such steps would read on the claimed

step of "separating said bound receptor" when this terminology is given its broadest reasonable interpretation.

The teachings of Wang differ from the claimed invention in that the prior art methods involve first arraying the receptors on the extended solid phase, followed by contacting with the plurality of antibody-microsphere binders. By contrast, the instant claims require that the bound receptor (after exposure to binder) be arrayed onto the substrate.

However, the courts have ruled that changes in the sequence of adding ingredients or in the order of performing process steps is considered only routine expedient, and Applicant has not demonstrated criticality with regard to the order in which the receptors are contacted with binder and with the substrate. See MPEP 2144.04.

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention by first contacting the receptors of Wang with binder (antibody-coated microspheres), followed by arraying of bound receptor onto the solid phase support. Absent evidence of criticality, the selection of any order of performing process steps is *prima facie* obvious. Consequently, one of ordinary skill in the art would have found it obvious to select any order of contacting receptor, binder, and substrate out of the course of routine optimization.

With respect to claim 11, it is acknowledged that the claim requires the potential binder to be "untagged". However, the instant specification defines a "tagged" ligand as one that is "attached via one or more chemical bonds to a chemical portion that fluoresces when exposed to non-ionizing, ultraviolet radiation" (page 2, lines 27-30). Therefore, an "untagged" potential binder would be one that is not fluorescently tagged. See also the instant specification at page 3, lines 9-20, where "untagged" binders are discussed in terms of fluorescent tags. Since there is

nothing in this definition that would rule out attachment of moieties that fluorescence when exposed to *ionizing* radiation (i.e., X-rays), when the claims are given their broadest reasonable interpretation the antibody-microsphere binders of Wang may be considered “untagged” according to Applicant’s definition since they do not contain tags that fluorescence when exposed to non-ionizing, UV radiation, but rather contain metal elements that fluorescence when exposed to ionizing X-rays (as in the instant specification).

With respect to claims 2-5 and 12-15, Wang teaches detection of proteins (e.g. viral glycoproteins), which read on the instant claims as proteins are carbon-containing polymers of amino acids (see Wang at claims 20 and 40 and column 8, lines 4-36). Similarly, the antibodies taught by Wang read on claims 6-8, 10, 16-18, and 20 since antibodies are also proteins.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42 of copending Application No. 10/880,388. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '388 application also recites a method in which an unbound receptor is exposed to a solution comprising at least one potential binder (chemical) that binds to the receptor to form a complex (see especially claims 1 and 30). Binding is detected by X-ray fluorescence; in particular, the X-ray fluorescence of the potential binder is assessed by exciting a heavy element that is present in the chemical and the receptor and subtracting a baseline X-ray fluorescence signal due to the receptor alone before binding. The detection of X-ray fluorescence signal from the chemical-receptor complex reads on the instantly claimed step of detecting an X-ray fluorescence signal generated by "bound members". The bound receptor may be said to be separated by the above methods, in that the baseline signals from unbound receptor are subtracted from the signals from the bound receptor-chemical complex (see especially claim 1). Therefore, separation occurs as a result of the recited data processing methods.

Copending Application No. 10/880,388 recites that the receptor may be arrayed or deposited on a substrate and exposed to the chemical (see claim 30). However, the copending application differs from the instant claims in that it does not require that the receptor be first bound to the chemical and then arrayed onto the substrate.

However, the courts have ruled that changes in the sequence of adding ingredients or in the order of performing process steps is considered only routine expedient, and Applicant has not demonstrated criticality with regard to the order in which the receptors are contacted with binder and with the substrate. See MPEP 2144.04.

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention by first contacting the receptors of Copending Application No. 10/880,388 with the chemical, followed by deposition on the substrate. Absent evidence of criticality, the selection of any order of performing process steps is *prima facie* obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claims 1-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/974,156. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '156 application also recites a method in which a receptor is exposed to a potential binder (chemical) that has at least one heavy element and a complex between the receptor and chemical is allowed to form (see especially claim 1). The receptor-chemical may be arrayed (deposited) on a substrate, i.e., arraying the bound receptors (see claim 2). The X-ray fluorescence signal due to the heavy element in the chemical-receptor complex is then measured, and the signal due to the chemical is detected by determining the net X-ray signal, from which the baseline signal due to receptor only has been subtracted, as an indication of binding affinity (see especially claim 1). Although copending Application No. 11/974,156 does not specifically recite that the receptor is "unbound", given the absence of a specific or limiting definition of this term in the instant specification, this terminology may be reasonably interpreted as meaning that the receptor is not yet bound to the chemical.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

21. Applicant's arguments filed 6/30/08 have been fully considered.
22. Applicant argues that the Examiner has failed to consider Applicant's arguments regarding the rejections of claims 1-20 under § 103(a) as being unpatentable over Pirrung et al. in view of Wang et al. (US 4,436,826) and refers to the Examiner's statements in the previous Office action that "Applicant's arguments with respect to claims 1-20 have been considered but are moot in view of the new ground(s) of rejection" (Office action mailed 1/28/08 at page 11). See Reply, page 6. The Examiner maintains that arguments regarding withdrawn rejections are of no legal significance.

Applicant also argues that the new grounds of rejection are improper because no amendments were made to the claims in the last response, and because "full faith and credit should be given to the search and action of a previous examiner unless there is a clear error in the previous action or knowledge of other prior art" (Reply, page 6). This is not found persuasive because the Examiner is unaware of any legal precedent for withdrawing rejections on such a basis. Applicant refers to the case of Amgen, Inc. v. Hoechst Marion Roussel, Inc. Although the issue of giving full faith and credit to a previous Examiner's search was discussed therein, the facts of that case differ and do not establish any basis for characterizing rejections as improper and/or withdrawing rejections made by a subsequent Examiner simply because a new search was made.

23. With respect to the rejections of claims 1-8, 10-18, and 20 under 35 U.S.C. 102(b) as being anticipated by Wang (US 4,663,277) in light of Plester et al., it is noted that the rejections have been obviated by the amendments to refer to method steps in the context of "bound" and "unbound" receptor(s). However, the claims remain unpatentable over the Wang reference for reasons discussed in detail above under § 103.

Applicant argues that Wang first arrays the receptors on the substrate followed by contacting with binder (see Reply, page 9). Applicant urges patentability on the basis of the order in which the receptors are contacted with the substrate and binder, but has not advanced evidence of criticality. Applicant's arguments alone are not persuasive because as discussed in detail above, it would have been obvious to select any order of contacting substrate, receptor, and binder since changing the sequence of adding ingredients or of performing process steps is considered routine expedient. See MPEP 2144.04.

Applicant further argues with respect to claim 11 that the terminology "untagged" means elements that are chemically associated and that are intrinsically integral to the component being measured (Reply, pages 10-11). This is not found persuasive because no such definition could be found in the instant specification, which defines a "tagged" ligand as being attached via one or more chemical bonds to a chemical portion that fluoresces when exposed to non-ionizing, ultraviolet radiation. See specification, page 2, lines 27-30. Because the binders of Wang would not be considered to be "tagged" according to Applicant's disclosed definition, it is maintained for reasons of record that the reference reads on the claim when given its broadest reasonable interpretation.

Application also points to the Declarations filed 10/19/07 of Drs. Warner and Havrilla et al. (see Reply, page 11). These Declarations were submitted in regards to rejections that have been since withdrawn, and relate to the teachings of different references. However, as best understood, Applicant wishes to underscore the above arguments that Wang involves the use of tagged, rather than untagged binders. The opinion evidence has been considered but is not persuasive because as discussed above, the Examiner finds that the specification does not support the narrow interpretation of the terminology “untagged” that Applicant is arguing.

24. With respect to the rejections of claims 1-5, 9-15, and 19-20 under 35 U.S.C. 102(c) as being anticipated by Sano et al. (US 6,391,590 B1), Applicant’s arguments (Reply, pages 12-13) have been fully considered but are not persuasive of error.

25. Applicant argues that Sano does not teach the detection of X-ray fluorescence from a bound receptor-binder complex (Reply, page 12, last paragraph), which is not on point because the claims do not recite or clearly require such a step. Claims 1 and 11 refer only to detection of an X-ray fluorescence signal in “bound members”. Nonetheless, Sano does teach detection of X-ray fluorescence from a bound receptor-binder complex, namely from chimeric protein (receptor) bound to cadmium heavy metal ion (binder). See Example 3.

Applicant also argues that Sano detects X-ray fluorescence from a tag rather than directly from a binder. Applicant argues that the heavy metal ion cadmium as taught by Sano et al. is a tag and not a binder. See Reply, the section bridging pages 12-13.

This is not found persuasive because Sano clearly teaches detection of X-ray fluorescence due to the heavy metal ion, in this case cadmium. Because cadmium binds to the chimeric

protein receptor, it reads on Applicant's claimed binder. Indeed, as recited in instant claims 9 and 19, heavy metal ions can indeed serve as binders according to the instant invention.

Applicant further argues that the claimed invention measures elements that are chemically associated and that are intrinsically integral to the component being measured (Reply, page 13). This is not found persuasive because such limitations are not recited in the claims. In any event, cadmium may be said to be "chemically associated and that are intrinsically integral to the component being measured" since it is one and the same as what is being measured by Sano.

Applicant also points to the Declarations submitted by Drs. Warner and Havrilla. However, as noted above, the Declarations provide opinions regarding no-longer-pending rejections made over different references. It is unclear what import the Declarations are believed to have with respect to the Sano et al. reference. While the opinion evidence therein has been considered, insufficient evidence is seen therein to support Applicant's position that the metal ions taught by Sano et al. may not be considered untagged binders, especially given that instant claims 9 and 19 indicate to the contrary.

26. With respect to the provisional double patenting rejections, Applicant argues that the currently pending claims as amended are patentably distinct from copending Application Nos. 10/880,388 and 11/974,156 (Reply, page 14). Such arguments are not persuasive because they do not point out the specific distinctions believed to render the claims patentably distinct, and therefore do not comply with CFR 1.111.

Conclusion

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached at (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine Foster/
Examiner, Art Unit 1641

/Mark L. Shibuya, Ph.D./
Supervisory Patent Examiner, Art Unit 1641